

What is claimed is:

Sub 1
1. A compound wherein a residue of a compound of formula I (Figure 1) is linked to a residue of a molecule comprising B-10, wherein X is CN, OH, CH₃, adenosyl, or a molecule comprising B-10; or a pharmaceutically acceptable salt thereof.

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2. The compound of claim 1 wherein the residue of a molecule comprising B-10 is directly linked to the 6-position of the compound of formula I or is directly linked to a residue of the b, d or e-carboxamide group of the compound of formula I.

3. The compound of claim 1 wherein the residue of a molecule comprising B-10 is linked by a linker to the 6-position of the compound of formula I or is linked by a linker to the residue of a-, b-, d- or e-carboxamide group of the compound of formula I.

4. The compound of claim 1 wherein the residue of a molecule comprising B-10 is linked to a residue of the b-carboxamide group of the compound of formula I.

5. The compound of claim 1 wherein the residue of a molecule comprising B-10 is linked to a residue of d-carboxamide group of the compound of formula I.

6. The compound of claim 1 wherein the residue of a molecule comprising B-10 is linked to a residue of the e-carboxamide group of the compound of formula I.

7. The compound of claim 1 wherein a residue of a molecule comprising B-10 is linked to a residue of the b-carboxamide group and a second residue of a molecule comprising B-10 is linked to a residue of the d-carboxamide group of the compound of formula I.

8. The compound of claim 1 wherein the residue of a molecule comprising B-10 is linked to the 6-position of the compound of formula I.

9. The compound of claim 1 wherein the molecule comprising B-10 contains 1 to about 20 boron atoms, inclusive.

10. The compound of claim 1 wherein the molecule comprising B-10 is an amino acid, a carbohydrate, a nucleoside or a carborane.

11. The compound of claim 1 wherein the molecule comprising B-10 is o-carborane, m-carborane or p-carborane.

12. The compound of claim 1 wherein the molecule comprising B-10 is o-carborane.

13. The compound of claim 3 wherein at least one linker is of the formula W-A-Q wherein A is (C₁-C₆)alkyl, (C₂-C₆)alkenyl, (C₂-C₆)alkynyl, (C₃-C₈)cycloalkyl, or (C₆-C₁₀)aryl, wherein W and Q are each independently -N(R)C(=O)-, -C(=O)N(R)-, -OC(=O)-, -C(=O)O-, -O-, -S-, -S(O)-, -S(O)₂-, -N(R)-, -C(=O)-, or a direct bond; wherein each R is independently H or (C₁-C₆)alkyl.

14. The compound of claim 13 wherein W is NH₂ or COOH and Q is NH₂ or COOH.

15. The compound of claim 13 wherein A is (C₁-C₆)alkyl.

16. The compound of claim 3 wherein at least one linker is about 5 angstroms to about 50 angstroms, inclusive.

17. The compound of claim 3 wherein at least one linker comprises a therapeutic radionuclide or a diagnostic radionuclide.

18. The compound of claim 17 wherein the therapeutic radionuclide is a metallic radionuclide.

19. The compound of claim 17 wherein the diagnostic radionuclide is a metallic radionuclide.

20. The compound of claim 17 wherein the diagnostic radionuclide is a non-metallic radionuclide.

21. The compound of claim 3 wherein at least one linker is a divalent radical formed from a peptide.

22. The compound of claim 3 wherein at least one linker is a divalent radical formed from an amino acid.

23. The compound of claim 3 wherein at least one linker is poly-L-glutamic acid, poly-L-aspartic acid, poly-L-histidine, poly-L-ornithine, poly-L-serine, poly-L-threonine, poly-L-tyrosine, poly-L-lysine-L-phenylalanine, poly-L-lysine or poly-L-lysine-L-tyrosine.

24. The compound of claim 1 wherein the residue of the compound of formula I is also linked to a linker comprising a detectable radionuclide or a therapeutic radionuclide.

25. A compound wherein a residue of a compound of formula I (Figure 1) is linked to a group of the formula Q-L-W-Det; wherein X is CN, OH, CH₃, adenosyl, a molecule comprising B-10, or Q-L-W-Det; wherein Det is a chelating group comprising Gd-157; L is a linker or absent; and W and Q are each independently -N(R)C(=O)-,

-C(=O)N(R)-, -OC(=O)-, -C(=O)O-, -O-, -S-, -S(O)-, -S(O)₂-, -C(=O)-, -N(R)-, or a direct bond; wherein each R is independently H or (C₁-C₆)alkyl; or a pharmaceutically acceptable salt thereof.

26. The compound of claim 25 wherein the group of the formula Q-L-W-Det is linked to a residue of the b-carboxamide group, a residue of the d-carboxamide group, a residue of the e-carboxamide, or the 6-position of the compound of formula I.

27. The compound of claim 25 wherein the group of the formula Q-L-W-Det is linked to a residue of the b-carboxamide group and a second group of the formula Q-L-W-Det is linked to a residue of the d-carboxamide group of the compound of formula I.

28. The compound of claim 25 wherein the group of the formula Q-L-W-Det is between about 20 and about 500 angstroms, inclusive, in length.

29. The compound of claim 25 wherein at least one chelating group is EDTA, DTPA, DOTA, DOTMP, TETA, MAG₃ or DCTA.

30. The compound of claim 25 wherein at least one chelating group is DTPA comprising Gd-157.

31. A compound wherein a residue of a compound of formula I (Figure 1) is linked to a residue of a molecule comprising B-10; wherein a residue of the compound of formula I is also linked to a group of the formula Q-L-W-Det, wherein X is CN, OH, CH₃, adenosyl, a group of the formula Q-L-W-Det, or a molecule comprising B-10; wherein:

Det is a chelating group comprising a therapeutic radionuclide or a diagnostic radionuclide;

L is a linker or absent; and

Q and W are each independently -N(R)C(=O)-, -C(=O)N(R)-, -OC(=O)-, -C(=O)O-, -O-, -S-, -S(O)-, -S(O)₂-, -C(=O)-, -N(R)-, or a direct bond; wherein each R is independently H or (C₁-C₆)alkyl; or a pharmaceutically acceptable salt thereof.

32. The compound of claim 31 wherein at least one of the radionuclides is $\text{Tc}^{99\text{m}}$, In^{111} , In^{110} , Gd^{157} or Y^{86} .

33. The compound of claim 31 wherein a molecule comprising B-10 is linked to the residue of a b-carboxamide group, d-carboxamide group, e-carboxamide group, or the 6-position of the compound of formula I.

34. The compound of claim 31 wherein the chelating group is DTA, DTPA, DOTA, TETA, DOTMP, MAG3 or DCTA.

35. The compound of claim 31 wherein the chelating group is DTPA.

36. The compound of claim 31 wherein the residue of a molecule comprising B-10 contains 1 to about 20 boron atoms.

37. The compound of claim 31 wherein the molecule comprising B-10 is a carbohydrate, an amino acid, a nucleoside or a carborane.

38. The compound of claim 31 wherein the molecule comprising B-10 is o-nido-carborane, m-nido-carborane or p-nido-carborane.

39. The compound of claim 31 wherein the molecule comprising B-10 is o-carborane.

40. The compound of claim 31 wherein the residue of a molecule comprising B-10 is directly linked to the 6-position or to the residue of the b-, d- or e-carboxamide group of the compound of formula I.

41. The compound of claim 31 wherein the residue of the compound of formula I is linked to a residue of a molecule comprising B-10 through a linker.

42. The compound of claim 41 wherein the linker comprises a non-metallic radionuclide.

43. The compound of claim 41 wherein the linker is about 5 angstroms to about 50 angstroms, inclusive.

44. The compound of claim 1 further comprising a detectable radionuclide.

Sub. 4 45. ~~The compound of claim 2 wherein the detectable radionuclide is a non-metallic radionuclide.~~

46. The compound of claim 3 wherein the non-metallic radionuclide is Carbon-11, Fluorine-18, Bromine-76, Iodine-123, or Iodine-124.

47. The compound of claim 2 wherein the detectable radionuclide is directly linked to the compound of formula I.

48. The compound of claim 2 wherein the detectable radionuclide is linked by a linker to the compound of formula I.

49. The compound of claim 6 wherein the linker is of the formula W-A wherein A is (C₁-C₆)alkyl, (C₂-C₆)alkenyl, (C₂-C₆)alkynyl, (C₃-C₈)cycloalkyl, or (C₆-C₁₀)aryl, wherein W is -N(R)C(=O)-, -C(=O)N(R)-, -OC(=O)-, -C(=O)O-, -O-, -S-, -S(O)-, -S(O)₂-, -N(R)-, -C(=O)-, or a direct bond; wherein each R is independently H or (C₁-C₆)alkyl; and wherein A is substituted with one or more non-metallic radionuclides.

50. The compound of claim 48 wherein the linker is about 5 angstroms to about 50 angstroms, inclusive.

51. The compound of claim 48 wherein the linker is a divalent peptide or amino acid.

52. The compound of claim 48 wherein the linker is poly-L-glutamic acid, poly-L-aspartic acid, poly-L-histidine, poly-L-ornithine, poly-L-serine, poly-L-threonine, poly-L-tyrosine, poly-L-lysine-L-phenylalanine, or poly-L-lysine or poly-L-lysine-L-tyrosine.

2/B211
53. The compound of claim 48 wherein the linker is linked to the 6-position of the compound of formula I or is linked to the residue of a-, b-, d- or e-carboxamide group of the compound of formula I.

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54. A compound wherein a residue of a compound of formula I (Figure 1) is linked 1) to a detectable radionuclide; and is linked 2) to a group comprising Gd-157; or a pharmaceutically acceptable salt thereof.

55. The compound of claim 54 wherein the group comprising Gd-157 has the formula Q-L-W-Det; wherein X is CN, OH, CH₃, adenosyl, a molecule comprising B-10, or Q-L-W-Det; Det is a chelating group comprising Gd-157; L is a linker or absent; and W and Q are each independently -N(R)C(=O)-, -C(=O)N(R)-, -OC(=O)-, -C(=O)O-, -O-, -S-, -S(O)-, -S(O)₂-, -C(=O)-, -N(R)-, or a direct bond, wherein each R is independently H or (C₁-C₆)alkyl.

56. The compound of claim 54 wherein the detectable radionuclide is a non-metallic radionuclide.

57. The compound of claim 56 wherein the non-metallic radionuclide is Carbon-11, Fluorine-18, Bromine-76, Iodine-123, or Iodine-124.

58. The compound of claim 54 wherein the detectable radionuclide is directly linked to the compound of formula I.

59. The compound of claim 54 wherein the detectable radionuclide is linked by a linker to the compound of formula I.

60. The compound of claim 59 wherein the linker is of the formula W-A wherein A is (C₁-C₆)alkyl, (C₂-C₆)alkenyl, (C₂-C₆)alkynyl, (C₃-C₈)cycloalkyl, or (C₆-C₁₀)aryl, wherein W is -N(R)C(=O)-, -C(=O)N(R)-, -OC(=O)-, -C(=O)O-, -O-, -S-, -S(O)-, -S(O)₂-, -N(R)-, -C(=O)-, or a direct bond; wherein each R is independently H or (C₁-C₆)alkyl; and wherein A is substituted with one or more non-metallic radionuclides.

61. The compound of claim 59 wherein the linker is about 5 angstroms to about 50 angstroms, inclusive.

62. The compound of claim 59 wherein the linker is a divalent peptide or amino acid.

63. The compound of claim 59 wherein the linker is poly-L-glutamic acid, poly-L-aspartic acid, poly-L-histidine, poly-L-ornithine, poly-L-serine, poly-L-threonine, poly-L-tyrosine, poly-L-lysine-L-phenylalanine, or poly-L-lysine or poly-L-lysine-L-tyrosine.

64. The compound of claim 59 wherein the linker is linked to the 6-position of the compound of formula I or is linked to the residue of a-, b-, d- or e-carboxamide group of the compound of formula I.

65. A compound wherein a residue of a compound of formula I (Figure 1) is linked 1) to a molecule comprising B-10 or to a chelating group comprising Gd-157, and 2) to at least one residue of the formula Q-L-W-Det; wherein each Det is independently a chelating group comprising a metallic radionuclide; each L is independently a linker or absent; and each W and Q is independently -N(R)C(=O)-, -C(=O)N(R)-, -OC(=O)-,

~~-C(=O)O-, -O-, -S-, -S(O)-, -S(O)₂-, -C(=O)-, -N(R)-, or a direct bond, wherein each R is independently H or (C₁-C₆)alkyl; or a pharmaceutically acceptable salt thereof.~~

66. The compound of claim 1 or 44 wherein the residue of a compound of formula I is also linked to a group comprising Gd-157.

67. The compound of claim 66 wherein the group comprising Gd-157 has the formula Q-L-W-Det; wherein X is CN, OH, CH₃, adenosyl, a molecule comprising B-10, or Q-L-W-Det; Det is a chelating group comprising Gd-157; L is a linker or absent; and W and Q are each independently -N(R)C(=O)-, -C(=O)N(R)-, -OC(=O)-, -C(=O)O-, -O-, -S-, -S(O)-, -S(O)₂-, -C(=O)-, -N(R)-, or a direct bond; wherein each R is independently H or (C₁-C₆)alkyl.

68. A pharmaceutical composition comprising a compound of any one of claims 1-67 and a pharmaceutically acceptable carrier.

69. A method of treating a tumor in a mammal in need of such treatment comprising administering to the mammal an effective amount of a compound of any one of claims 1-67 in combination with a pharmaceutically acceptable vehicle; and administering neutron capture therapy.

70. A method for imaging a tumor in a mammal comprising administering to the mammal a detectable amount of a compound of any one of claims 1-67; and detecting the presence of the compound.

71. The method of claim 70 further comprising treating the tumor with neutron capture therapy.

72. A compound of any one of claims 1-67 for use in medical therapy or diagnosis.

~~The use of a compound of any one of claims 1-67 for the manufacture~~

~~of a medicament for imaging a tumor in a mammal.~~

The use of a compound of any one of claims 1-67 for the manufacture

of a medicament for treating a tumor in a mammal in need of such treatment.

Questions are asked about the effect of the new rules on the market for derivatives.